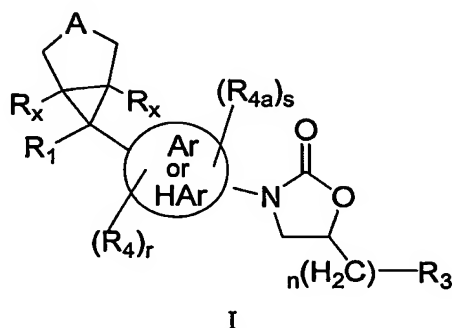


WHAT IS CLAIMED IS:

1. The present invention relates to compounds of formula I:

5



its enantiomer, diastereomer, or pharmaceutically acceptable salt, hydrate or prodrug thereof
 10 wherein:

R₁ represents

- vi) hydrogen,
- vii) NR₅R₆,
- 15 viii) CR₇R₈R₉, C(R)₂OR₁₄, CH₂NHR₁₄,
- ix) C(=O)R₁₃, C(=NOH)H, C(=NOR₁₃)H, C(=NOR₁₃)R₁₃, C(=NOH)R₁₃, C(=O)N(R₁₃)₂,
 C(=NOH)N(R₁₃)₂, NHC(=X₁)N(R₁₃)₂, (C=NH)R₇, N(R₁₃)C(=X₁)N(R₁₃)₂, COOR₁₃,
 SO₂R₁₄, N(R₁₃)SO₂R₁₄, N(R₁₃)COR₁₄,
- x) (C₁₋₆alkyl)CN, CN, CH=C(R)₂, (CH₂)_pOH, C(=O)CHR₁₃, C(=NR₁₃)R₁₃,
 20 NR₁₀C(=X₁)R₁₃; or

vi) C₅₋₁₀ heterocycle optionally substituted with 1-3 groups of R₇, which may be attached
 through either a carbon or a heteroatom;

25 A represents NR, O, or S(O)_p;



represents aryl or heteroaryl, heterocycle, heterocyclyl or heterocyclic, provided that in the case of a heteroaryl, heterocycle, heterocyclyl or heterocyclic, the cyclopropyl is not attached to a nitrogen atom on the ring;

5 R_x represents hydrogen or C_{1-6} alkyl;

R_3 represent

- i) $NR_{13}(C=X_2)R_{12}$,
- ii) $NR_{13}(C=X_1)R_{12}$,
- 10 iii) $NR_{13}SO_2R_{14}$,
- iv) $N(R_{13})\text{heteroaryl}$,
- v) $NR_{13}(CHR_{13})_{0-4}\text{aryl}$,
- vi) $NR_{13}(CHR_{13})_{0-4}\text{heteroaryl}$,
- vii) $S(CHR_{13})_{0-4}\text{aryl}$,
- 15 viii) $S(CHR_{13})_{0-4}\text{heteroaryl}$,
- ix) $O(CHR_{13})_{0-4}\text{aryl}$,
- x) $O(CHR_{13})_{0-4}\text{heteroaryl}$,
- xi) $NOH(C=X_1)R_{12}$,
- xii) $-OC=N(OCO\text{aryl}) C_{1-6} \text{ alkyl}$
- 20 xiii) $-OC=N(OH) C_{1-6} \text{ alkyl}$
- xiv) $C_{5-10} \text{ heteroaryl}$ which may be attached through either a carbon or a heteroatom; said aryl and heteroaryl optionally substituted with 1-3 groups of R_7 ,

R_4 , and R_{4a} , independently represent

- 25 v) hydrogen,
- vi) halogen,
- vii) C_{1-6} alkoxy, or
- viii) C_{1-6} alkyl

30 r and s independently are 1-3, with the provision that when $(R_{4a})_s$ and $(R_4)_r$ are attached to an Ar or HAr ring the sum of r and s is less than or equal to 4;

R₅ and R₆ independently represent

- xiii) hydrogen,
- xiv) C₁₋₆ alkyl optionally substituted with 1-3 groups of halogen, CN, OH, C₁₋₆ alkoxy, amino, imino, hydroxyamino, alkoxyamino, C₁₋₆ acyloxy, C₁₋₆ alkylsulfenyl, C₁₋₆ alkylsulfinyl, C₁₋₆ alkylsulfonyl, aminosulfonyl, C₁₋₆ alkylaminosulfonyl, C₁₋₆ dialkylaminosulfonyl, 4-morpholinylsulfonyl, phenyl, pyridine, 5-isoxazolyl, ethylenyloxy, or ethynyl, said phenyl and pyridine optionally substituted with 1-3 halogen, CN, OH, CF₃, C₁₋₆ alkyl or C₁₋₆ alkoxy;
- xv) C₁₋₆ acyl optionally substituted with 1-3 groups of halogen, OH, SH, C₁₋₆ alkoxy, naphthalenoxy, phenoxy, amino, C₁₋₆ acylamino, hydroxylamino, alkoxyamino, C₁₋₆ acyloxy, aralkyloxy, phenyl, pyridine, C₁₋₆ alkylcarbonyl, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, C₁₋₆ hydroxyacyloxy, C₁₋₆ alkylsulfenyl, phthalimido, maleimido, succinimido, said phenoxy, phenyl and pyridine optionally substituted with 1-3 groups of halo, OH, CN, C₁₋₆ alkoxy, amino, C₁₋₆ acylamino, CF₃ or C₁₋₆ alkyl;
- xvi) C₁₋₆ alkylsulfonyl optionally substituted with 1-3 groups of halogen, OH, C₁₋₆ alkoxy, amino, hydroxylamino, alkoxyamino, C₁₋₆ acyloxy, or phenyl; said phenyl optionally substituted with 1-3 groups of halo, OH, C₁₋₆ alkoxy, amino, C₁₋₆ acylamino, CF₃ or C₁₋₆ alkyl;
- xvii) arylsulfonyl optionally substituted with 1-3 of halogen, C₁₋₆ alkoxy, OH or C₁₋₆ alkyl;
- xviii) C₁₋₆ alkoxy carbonyl optionally substituted with 1-3 of halogen, OH, C₁₋₆ alkoxy, C₁₋₆ acyloxy, or phenyl, said phenyl optionally substituted with 1-3 groups of halo, OH, C₁₋₆ alkoxy, amino, C₁₋₆ acylamino, CF₃ or C₁₋₆ alkyl;
- xix) aminocarbonyl, C₁₋₆ alkylaminocarbonyl or C₁₋₆ dialkylaminocarbonyl, said alkyl groups optionally substituted with 1-3 groups of halogen, OH, C₁₋₆ alkoxy or phenyl
- xx) five to six membered heterocycles optionally substituted with 1-3 groups of halogen, OH, CN, amino, C₁₋₆ acylamino, C₁₋₆ alkylsulfonylamino, C₁₋₆ alkoxy carbonylamino, C₁₋₆ alkoxy, C₁₋₆ acyloxy or C₁₋₆ alkyl, said alkyl optionally substituted with 1-3 groups of halogen, or C₁₋₆ alkoxy;
- xxi) C₃₋₆ cycloalkylcarbonyl optionally substituted with 1-3 groups of halogen, OH, C₁₋₆ alkoxy or CN;
- xxii) benzoyl optionally substituted with 1-3 groups of halogen, OH, C₁₋₆ alkoxy, C₁₋₆ alkyl, CF₃, C₁₋₆ alkanoyl, amino or C₁₋₆ acylamino;
- xxiii) pyrrolylcarbonyl optionally substituted with 1-3 of C₁₋₆ alkyl;

- xxiv) C1-2 acyloxyacetyl where the acyl is optionally substituted with amino, C1-6 alkylamino, C1-6 dialkylamino, 4-morpholino, 4-aminophenyl, 4-(dialkylamino)phenyl, 4-(glycylamino)phenyl; or
- R5 and R6 taken together with any intervening atoms can form a 3 to 7 membered
- 5 heterocyclic ring containing carbon atoms and 1-2 heteroatoms independently chosen from O, S, SO, SO₂, N, or NR₈;
- R7 represent
- iii) hydrogen, halogen, CN, CO₂R, CON(R)₂, CHO, CH₂NHAc, C(=NOR), OH, C1-6
- 10 alkoxy, C1-6 alkyl, alkenyl, hydroxy C1-6 alkyl, (CH₂)₁₋₃NHC(O)C1-6 alkyl, (CH₂)₁₋₃N(C1-6 alkyl)₂
- iv) (CH₂)_namino, (CH₂)_nC1-6 alkylamino, C1-6 dialkylamino, hydroxylamino or C1-2 alkoxyamino all of which can be optionally substituted on the nitrogen with C1-6 acyl, C1-6 alkylsulfonyl or C1-6 alkoxycarbonyl, said acyl and alkylsulfonyl
- 15 optionally substituted with 1-2 of halogen or OH;
- R8 and R9 independently represents
- iv) H, CN,
- v) C1-6 alkyl optionally substituted with 1-3 halogen, CN, OH, C1-6 alkoxy, C1-6
- 20 acyloxy, or amino,
- vi) phenyl optionally substituted with 1-3 groups of halogen, OH, C1-6 alkoxy; or
- R7 and R8 taken together can form a 3-7 membered carbon ring optionally interrupted with
- 1-2 heteroatoms chosen from O, S, SO, SO₂, NH, and NR₈;
- 25 X₁ represents O, S or NR₁₃, NCN, NCO₂R₁₆, or NSO₂R₁₄
- X₂ represents O, S, NH or NSO₂R₁₄;
- 30 R₁₀ represents hydrogen, C1-6 alkyl or CO₂R₁₅;
- R₁₂ represents hydrogen, C1-6 alkyl, NH₂, OR, CHF₂, CHCl₂, CR₂Cl, (CH₂)_nSR, (CH₂)_nCN, (CH₂)_nSO₂R, (CH₂)_nS(O)R, C1-6 alkylamino, C5-10 heteroaryl or C1-6 dialkylamino, where

said alkyl may be substituted with 1-3 groups of halo, CN, OH or C₁₋₆ alkoxy, said heteroaryl optionally substituted with 1-3 groups of R₇;

- Each R₁₃ represents independently hydrogen, C₁₋₆ alkyl, C₆₋₁₀ aryl, NR₅R₆, SR₈, S(O)R₈,
 5 S(O)₂R₈, CN, OH, C₁₋₆ alkylS(O)R, C₁₋₆ alkoxy carbonyl, hydroxycarbonyl, -OCOaryl, C₁₋₆ acyl, C₃₋₇ membered carbon ring optionally interrupted with 1-4 heteroatoms chosen from O, S, SO, SO₂, NH and NR₈ where said C₁₋₆ alkyl, aryl or C₁₋₆ acyl groups may be independently substituted with 0-3 halogens, hydroxy, N(R)₂, CO₂R, C₆₋₁₀ aryl, C₅₋₁₀ heteroaryl, or C₁₋₆ alkoxy groups;
 10 When two R₁₃ groups are attached to the same atom or two adjacent atoms they may be taken together to form a 3-7 membered carbon ring optionally interrupted with 1-2 heteroatoms chosen from O, S, SO, SO₂, NH, and NR₈;

R represents hydrogen or C₁₋₆ alkyl;

- 15 R₁₄ represents amino, C₁₋₆ alkyl, C₁₋₆ haloalkyl, five to six membered heterocycles or phenyl, said phenyl and heterocycles optionally substituted with 1-3 group of halo, C₁₋₆ alkoxy, C₁₋₆ acylamino, or C₁₋₆ alkyl, hydroxy and/or amino, said amino and hydroxy optionally protected with an amino or hydroxy protecting group;

- 20 R₁₅ is C₁₋₆ alkyl or benzyl said benzyl optionally substituted with 1-3 groups of halo, OH, C₁₋₆ alkoxy, amino, C₁₋₆ acylamino, or C₁₋₆ alkyl;

- R₁₆ is hydrogen, C₅₋₁₀ heteroaryl, C₆₋₁₀ aryl, said heteroaryl and aryl optionally substituted
 25 with 1-3 groups of R₇;

p represents 0-2 and

m, n, and q represents 0-1.


30

2. A compound according to claim 1 wherein R₁ represents H, NR₅R₆, CN, OH, C(R)₂OR₁₄, NHC(=X₁)N(R₁₃)₂, C(=NOH)N(R₁₃)₂, NR₁₀C(=X₁)R₁₃ or CR₇R₈R₉.



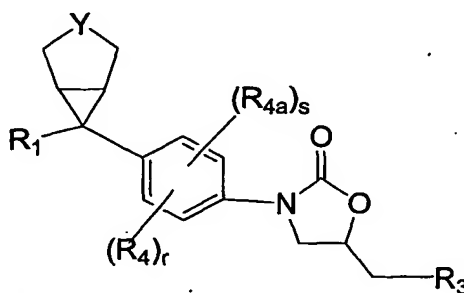
3. A compound according to claim 1 wherein is phenyl, pyridine, pyrimidine, or piperidine.

4. A compound according to claim 3 wherein R_1 is NR_5R_6 , or CN and R_3 is $NR_{10}C(=X_1)R_{13}$, $NR(C=X_1)R_{12}$, C_{5-10} heteroaryl, $NH(CH_2)_{0-4}$ aryl, $NH(CH_2)_{0-4}$ heteroaryl, said aryl and heteroaryl optionally substituted with 1-3 groups of R_a .

5. A compound according to claim 3 wherein R_3 is a C_{5-10} heteroaryl represented by  which represents an optionally substituted aromatic heterocyclic group containing 1 to 4 nitrogen atoms and at least one double bond, and which is connected through a bond on any nitrogen.

6. A compound according to claim 1 wherein the structural formula is

II:



Formula II

wherein R_1 , R_4 , R_{4a} , Y and R_3 are as described above.

7. A compound which is:

N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-(6-cyanobicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

- 1-[5(R)-3-[4-[(1 α ,5 α ,6 β)-(6-cyanobicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,
N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-(3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
5 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-(6-cyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide ,
1-[5(R)-3-[4-[(1 α ,5 α ,6 β)-(3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole,
1-[5(R)-3-[4-[(1 α ,5 α ,6 β)-(6-cyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]-1,2,3-triazole ,
10 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-(3-acetoxyacetyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-(6-cyano-3-hydroxyacetyl-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
15 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-(6-cyano-3-methanesulfonyl-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-(6-cyano-3-methyl-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-(3,6-dicyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
20 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-(6-cyano-3-cyanomethyl-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
5(R)-3-[4-[(1 α ,5 α ,6 β)-(3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-5-[(isoxazol-3-yl)oxy]methyloxazolidin-2-one,
25 5(R)-3-[4-[(1 α ,5 α ,6 β)-(6-cyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-5-[(isoxazol-3-yl)oxy]methyloxazolidin-2-one ,
5(R)-3-[4-[(1 α ,5 α ,6 β)-(3-t-butoxycarbonyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-5-[N-(t-butoxycarbonyl)-N-(isoxazol-3-yl)]aminomethyloxazolidin-2-one,
5(R)-3-[4-[(1 α ,5 α ,6 β)-(6-cyano-3-azabicyclo[3.1.0]hexan-6-yl)]phenyl]-5-[N-(isoxazol-3-yl)]aminomethyloxazolidin-2-one,
30 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-(5-cyanopyridin-2-yl)-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-(pyridin-2-yl)-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,

- N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[3-acetyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-(pyrimidin-2-yl)-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- 5 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-(4-pyridylmethyl)-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-(N-cyano-1-iminoethyl)-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-methoxycarbonyl-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- 10 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-(N-cyano-S-methylthioiminomethyl)-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-(N-cyanocarboxamidyl)-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- 15 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[3-(N,N'-t-butoxycarbonylcarboxamidyl)-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[3-carboxamidyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[3-(N-t-Butoxycarbonylamino)acetyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- 20 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[3-aminoacetyl-6-cyano-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-methanesulfonylacetyl-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- 25 N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-(dibenzylphosphoryloxy)acetyl-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- N-[5(S)-3-[4-[(1 α ,5 α ,6 β)-[6-cyano-3-(phosphoryloxy)acetyl-3-azabicyclo[3.1.0]hexan-6-yl]]phenyl]-2-oxooxazolidin-5-ylmethyl]acetamide,
- 30 or their enantiomer, diastereomer, or pharmaceutically acceptable salt, hydrate or prodrug thereof wherein.

8. A pharmaceutical composition comprised of a compound in accordance with claim 1 in combination with a pharmaceutically acceptable carrier

and optionally a in combination with a vitamin selected from the group consisting vitamin B2, vitamin B6, vitamin B12 and folic acid.

5 9. A method of treating or preventing a bacterial infection in a mammalian patient in need thereof, comprising administering to said patient an effective amount of a compound of claim 1.

10 10. A method of treating or preventing bacterial infection or an oxazolidinone-associated side effect by administering an effective amount of a compound of formula I of claim 1 and an effective amount of one or more of a vitamin selected from the group consisting of vitamin B2, vitamin B6, vitamin B12 and folic acid to a patient in need thereof.

15 11. A method according to claim 16 for treating or preventing oxazolidinone-associated normocytic anemia, peripheral sensory neuropathy, sideroblastic anemia, peripheral sensory neuropathy, optic neuropathy, seizures, thrombocytopenia, cheilosis, hypo-regenerative anemia, megaloblastic anemia and seborrheic dermatitis by administering an effective amount of vitamin B2 to a patient in need thereof.

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